UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,825	02/25/2002	Man Sung Co	011823-004012US	5851

7590 09/27/2004

TOWNSEND AND TOWNSEND AND CREW
379 LYTTON AVENUE
PALO ALTO, CA 94301-1431

EXAMINER
HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,825	CO ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1. The request filed on 7/19/04 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 10/084825 is acceptable and a RCE has been established. Claims 30-45 are pending and are currently under prosecution. An action on the RCE follows.

2. Claim 30, 32-45 have been amended.

3. Claims 30-45 are pending and under examination.

4. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

5. The following Office Action contains NEW GROUNDS of rejection.

Rejections Withdrawn

6. The rejection of Claims 36-37 under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description is withdrawn in view of the ATCC catalog showing HB-10306 is publicly available.

Response to Arguments

7. The rejection of claims 30-45 under 35 U.S.C. 112, first paragraph, is maintained.

The response filed 7/19/04 has been carefully considured but is deemed not to be persuasive. The response states that the specification provides the sequences for glycosylation and identifying which residues to substitute to result in an antibody with increased affinity does not require undue experimentation and sites Sox and Hood for showing only 20% of human antibodies are glycosylated in the V region and all one needs to test whether elimination of the glycosylation site results in increased affinity is to test for it (see page 8-9 of response). In response to this argument, while there may be 20% of antibodies that have glycosylation sites in the V region, and one can identify the sites, it is not routine to screen antibodies to obtain an outcome that is quite rare (see below). The response cites the WO 03/016466 reference for this reference teaches elimination of a glycosylation site in the CDR2 and the response states that all is needed to screen for increased affinity is routine just like screening antibodies from hybridomas (see page 10 of response). In response to this argument, while screening hybridomas for antibodies is routine because one has an expectation of obtaining an antibody, it is not routine to remove a glycosylation site and obtain an antibody that has an increased in affinity. As taught in the WO 03/016466 (IDS 7/19/04) reference "Quite unpredictable" the affinity of the antibody that is deglycosylated is higher (see page 3, lines 17-19) and "We have surprisingly found...surprisingly higher affinity than glycosylated mouse or humanized 266 antibodies" (see page 7, 25-30). Thus, the prior art teaches the unpredictability of obtaining an antibody with higher affinity by removing

a glycosylation site in the variable region even in the CDRs or frameworks. Just screening would not be routine because one has to expect to find what one is looking for which is not the case in this instance. It is unpredictable whether glycosylation would affect affinity, positively, negatively, or not at all as taught in WO 03/016466 (see page 3, lines 13-15). Therefore, one skill in the art could not predict without undue experimentation whether removal of ANY glycosylation site in ANY antibody would result in an increased affinity. It is not a question of screening, it is a question of whether one skill in the art could predict whether one would obtain such outcome and as evidenced from the prior art one would not expect or predict such outcome. Just because one can identify the residues that need to be substituted does not result in producing an antibody that has an increase in affinity compared to the parent antibody. In addition, as stated the specification does not teach mutations within the entire variable region and in fact the specification only has one example of altering residue 73 in a framework region of a CD33 antibody and this one example resulted in an increase in affinity compared to the parent. However, the claims encompass alterations in the entire variable region, including the CDRs and framework.

The specification provides no direction or guidance regarding how to produce antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

The following is a NEW GROUND of rejection

Claim Rejections - 35 USC § 112

8. Claims 30-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass an antibody with a glycosylation site removed and this results in increased affinity. The only antibody and example in the specification is modifying framework position 73 in the M195 antibody that resulted in increased affinity (see page 24). The specification has not described any other antibody or position in any other antibody that upon removal would result in an antibody with an increase in affinity or a representative number of species for the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed structure of the encompassed genus of antibodies, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew, can be reached at (571) 272-0787.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is 703-872-9306.

Larry R. Helms

571-272-0832

LARRY R. HELMS, PH.D
PRIMARY EXAMINER